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Evaluation of mutagenic activity of the organo-selenium compound Selol by use of the *Salmonella typhimurium* mutagenicity assay

I. Rahden-Staroń[a,*], P. Suchocki[b], H. Czeczot[a]

[a] Department of Biochemistry, Medical University of Warsaw, 02-097 Warszawa, Banacha 1, Poland
[b] Department of Drug Analysis, Medical University of Warsaw, 02-097 Warszawa, Banacha 1, Poland

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ABSTRACT

We examined the mutagenic activity of the anti-oxidant Selol, an organo-selenium compound, by use of the *Salmonella typhimurium* mutagenicity assay (Ames test) with strains TA97a, TA98, TA100, TA 1535 and TA102 in the absence and in the presence of metabolic activation with an S9 fraction from Aroclor-induced rat liver. Doses were 330, 500, 1000 and 5000 μg per plate. Selol contains the element selenium (valency, +4) in its structure and it may have chemopreventive and anticancer activity. Selol was found to be non-toxic and non-mutagenic for test doses up to 5% per plate (which designates the declared content of Selenium (+4) as 5000 μg per plate) in all the *S. typhimurium* strains.

1. Introduction

Selenium is a trace element necessary for the regular functioning of living organisms. It exists in several forms: the four natural oxidation states of selenium are elemental selenium (0), selenide (−2), selenite (+4), and selenate (+6). Inorganic selenate and selenite predominate in water, whereas organic selenium compounds (selenomethionine, selenocysteine) are the major selenium species in cereal and in vegetables. Both selenite and selenate possess substantial bio-availability. Selenium salts are toxic in large amounts, but trace quantities of the element are necessary for the cellular functions in animals, forming the active centre of the enzymes glutathione peroxidase and thioredoxin reductase (which indirectly reduce certain oxidized molecules in animals and some plants) and three known deiodinase enzymes (which convert one of the thyroid hormones to another). The toxicity of the different forms of selenium depends on the oxidation state of Se [1]. The highest biological activity as an anti-oxidant and anticancer agent is assigned to selenium compounds containing tetravalent Se (+4).

Selenite-triglycerides are a new semi-synthetic group of compounds containing selenium (+4). Selol is a mixture of selenite-triglycerides from sunflower oil (obtained as previously described [2]). The putative structure of Selol, elucidated on the basis of [^{1}H]- and [^{13}C]-NMR study is presented in Fig. 1. Selol did not show a cumulative toxicity in rats: during a long-term study, Selol was supplied to rats and no side effects were observed [3,4]. As Selol contains the element selenium in its structure, it is suspected to exhibit chemopreventive and anticancer activity. The ability of Selol to inhibit cell proliferation and to induce apoptosis was shown by Suchocki et al. [5] on leukemia HL-60 cells and multidrug-resistant HL-60/Dox and HL-60/Vinct cell lines. All cell lines studied proved to be sensitive to Selol. The substance overcame the drug resistance, as doxorubicin-resistant cells were more sensitive towards Selol than doxorubicin-sensitive cells. It has also been shown that the concomitant administration of Selol and opioids markedly enhanced the analgesic activity of some of the latter, thus it may be beneficial in terminal neoplastic states [6].

We considered it necessary to undertake a study to determine whether Selol shows any mutagenic activity and could be safely used for potential pharmaceutical purposes.

2. Materials and methods

2.1. Selol

Selol is a mixture of selenite-triglycerides, containing 0.5–5% (w/w) of Se (+4). It was obtained from sunflower oil in the Department of Drug Analysis at Warsaw Medical University [2]. The structure of Selol, based on [^{1}H]- and [^{13}C]-NMR studies, is presented in Fig. 1. The indication 0.5–5% (w/w) Selol refers to the actual content of selenium (+4) as 0.5% (w/w) to 5% (w/w), respectively.

2.2. Chemicals

The following chemicals were obtained from the sources listed below: Aroclor 1254 was from Analabs Inc.; mitomycin C, methyl methanesulfonate (MMS), sodium azide and 2-aminoanthracene were from Sigma; 2-aminofluorene from Aldrich; 1-oxide-4-nitroguinolone (4-NQO) and dimethyl

* Corresponding author. Tel.: +48 22 572 06 93; fax: +48 22 572 0679.
E-mail address: iwonna.rahden-staron@wum.edu.pl (I. Rahden-Staroń).

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